LONG-TERM PERCUTANEOUS ACCESS DEVICE

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The tendency of the skin to marsupialize around a penetrating foreign body, leading to subsequent infection, remains the major contributing factor to percutaneous access device (PAD) failure[1-4]. Various investigators have used different techniques in an attempt to form a seal between a PAD and the surrounding tissues to inhibit epidermal downgrowth and prevent the resultant infection[3,5,6].

Basal cells of the epidermis proliferate on but not through the dermis. It is believed that they are prevented from doing so by the presence of the collagenous network of the dermis[7]. The same physiological mechanism, we hypothesized, can prevent epithelial downgrowth along the device-tissue interface of a PAD.

To evoke this mechanism by our PAD, the implant surface is rendered nanoporous: that is, nonintercommunicating pores of one micron diameter and 20 μ depth are produced at a density of 15,000/mm^2. The implant is then coated with autologous dermal fibroblasts which interlock firmly with the nanoporous surface. This is accomplished in vitro (in a zero strain environment) using cell culture techniques under conditions that favor fibroblast proliferation followed by collagen synthesis and polymerization. The result is an Autologous, Living, COated, Nanoporous, or ALCON surface.

The merger of the cultured dermal cell layers on the PAD with the host dermis after implantation results in a "biological seal" which is impervious to fluids and microorganisms and acts as a physiological barrier to the migrating epithelial cells. Under these conditions, normal tissue repair is expected to take place in the region of the PAD-tissue interface. Thus, barring excessive trauma, the "seal" should last for the life of the host.

We previously reported[8] the histological results from our first group of swine which demonstrated the feasibility of inhibiting epithelial downgrowth along the ALCON PAD, kept in place for an average of 197 days.

In this paper, we: 1) present the current status of our long-term PAD implants in swine; 2) report on transferring the technique of PAD insertion to sheep; and 3) describe the results of a feasibility study of the initial steps required to replicate this technique for human use.

MATERIALS AND METHODS

After initial skin biopsy, enzymes are used to isolate the fibroblasts, which subsequently are subcultured onto the polycarbonate (Lexan 104, G.E. Schenectady, NY) sleeve of the PAD for about 2 wks[4]. During this time, the fibroblasts form cytoplasmic projections into the pores, produce a multilayer coating, and synthesize collagen. Upon implantation of the PAD into the swine, using one of the 2 previously described methods[9], these fibroblasts will be integrated with the dermis forming a seal strong enough to act as a barrier to epithelial downgrowth and bacterial invasion.

The design of the PAD model (patent pending) and its dimensions were described in a previous report[10]. It consists of various parts (Figure 1): a stainless steel core covered with Dacron velour, the flange; the Lexan sleeve, which forms the critical tissue interface, where the device pierces the skin; and an extension used to prevent overgrowth of the PAD by the skin (such an extension is necessitated by the fact that this version of the PAD is not attached to anything either externally or internally. It was designed specifically to test the ability of the ALCON surface to form a successful biological seal). The Lexan sleeve is rendered nanoporous by nuclear bombardment followed by sodium hydroxide etching.

Swine. A single PAD was implanted (surgical technique is described by Wasfie[9]) in each of the CSU 19 Yucatan miniature swine to evaluate long-term (2 yr) host-device interaction. There were 15 ALCON PADs in the current group and 4 controls (identical devices, but without the fibroblast coating). Except for a dry dressing applied weekly to keep the implant and its adjacent area clean, no topical or systemic medications were administered.

Sheep. To assess the feasibility of transferring the technique of cell culture and PAD insertion to sheep, 10 PADs were implanted in 5 female Suffolk sheep (weighing between 46-107 kg) and kept in place for a period of 5-8 wks. In 2 of these sheep, the PAD was attached to a subcutaneous pumping chamber and provisions were made for the passage of gas through the PAD. A harness encircled the neck, chest and front legs of each sheep. Looped and secured to the harness, the air tube from the PAD led from there to a swivel joint above the pen. Daily intermittent pumping was begun.

Human. To determine whether fibroblasts from older humans can be cultured by the same technique, biopsy samples were obtained from 7 patients (ranging from 42-77 yrs of age) undergoing elective surgery.

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TABLE I. CURRENT STATUS OF SWINE PADs (CONTROL)

PAD No.	Implant Duration (days)*	Status	Clinical Observation
38	215		Skin retracted from sleeve
39	238	Expl	Gross infection
40	145		Skin retracted from sleeve
52	185+	Expl	Explanted, swine died

*Implant duration to failure
+No clinical sign of failure
Expl = Explanted

TABLE II. CURRENT STATUS OF ALCON PAD IMPLANTS IN SWINE

PAD No.	Implant Duration (days)*	Status	Clinical Observation
10	186	Expl	Pressure necrosis of the skin by the flange
19	776+		
21	136+	Expl	Explanted following trauma
30	431	Expl	Pressure necrosis of the skin by the flange
31	499+	Expl	Animal died of leukemia
32	377+		
33	339	Expl	Broken sleeve
34	532+		
36	420		Detachment of the skin from the sleeve
37	201+		
41	633	Expl	Infection under the flange
46	615+		
48	517+		
49	517+		
55	314	Expl	Detachment of velour

*Implant duration to failure for PADs that failed with no clinical sign of failure or to 7/10/85 for implants
+No clinical sign of failure or infection
Expl = Explanted

RESULTS

Swine. Tables I and II show the status and outcome of PAD implants in the swine. Three out of 4 controls failed 5 to 7 mos postimplantation. One had to be removed following infection around the PAD (PAD No. 39). The remaining 2 (PAD Nos. 38 and 40) showed progressive sinus formation and skin retraction exposing the velour. Although the fourth control PAD did not show clinical signs of failure, it had to be explanted due to progressive weight loss by the swine, caused by a pyloric tumor which necessitated sacrifice of the animal.

Of the 15 ALCON PADs (Table II), 5 had to be explanted due to various technical problems. Two were removed due to material failure: PAD No. 33 following fracture of the sleeve, and PAD No. 55, following detachment of the velour, the cause of which is not yet determined. Two PADs (Nos. 10 and 30) failed because of an error in the surgical implantation technique. The fifth (PAD No. 21) was removed after trauma of unknown origin to the PAD. Histology of the interface showed the epithelial downgrowth halted at the junction of the sleeve and the extension (Figure 1).

Of the remaining 10 ALCON PADs, only 2 (PAD Nos. 36 and 41) showed deterioration with retraction of the skin from the sleeve, while all other ALCON PADs (duration of these range from 8-25 mos) are clinically satisfactory with no sign of infection or marsupialization. Considering only the 10 PADs that did not encounter technical problems, we find that the PAD failure rate (to July, 1985) is 1 every 82 implant-months, compared to 1 every 7 implant-months in the control group (Tables I and II).

Sheep. Ten PADs were implanted, 7 ALCON and 3 control. Five to 8 wks after implantation, 3 control and 5 ALCON PADs were removed en bloc and fixed in 10% buffered formaldehyde. The Lexan sleeve was dissolved in methylene chloride and the stainless steel skeleton of the PAD dissected to allow sectioning. Sections were taken at the 6 o'clock and 12 o'clock positions. The gross appearance showed bland fibrous tissue surrounding the PAD necks. There was some desquamated epithelium on the surface. Microscopically, there was evidence of foreign body reaction around the Dacron velour, and in some sections minimal acute inflammation surrounded the tract.

In the 3 controls, the epidermis had migrated 75%, 100%, and 00% of the dermal thickness, respectively (Figure 3). In contrast, with ALCON surfaced implants, the epidermis halted abruptly as it turned from the skin surface into the tract (Figure 4) in 5 of the 10 sections examined. In the others, the extent of migration was 10%, 20%, 25%, 33%, and 80%, respectively.

Clinical observation of the 2 sheep which have active (transmitting pneumatic power) PADs reveals no sign of infection or sinus formation to date, 4 mos postimplantation.

Human. All 7 specimens were successfully cultured onto Lexan. Our initial impressions are that human skin is technically easier to dissect (dermis from epidermis) than that of swine or sheep, and that obtaining a confluent culture as well as multilayered fibroblast growth, even from a 77 yr old donor, appears feasible.

DISCUSSION

When considering requirements for a successful PAD that would allow long-term access to the internal environment of the human body, certain criteria must be met. First, the natural defense mechanism of the skin to any penetrating foreign body, the tendency for marsupialization, must be overcome in order to achieve a stable long-lasting seal between the PAD and the surrounding tissues. Second, mechanical stress between the PAD and the surrounding tissue must be minimized to protect the bond between the cells and the PAD.

Our solution to the first, the ALCON surfaced PAD, which forms a seal when implanted, appears to be successful in inhibiting epithelial downward migration. Our solution to the second relies on a large subcutaneous Dacron velour covered flange to redirect stress away from the PAD-tissue interface[11].

Our PAD was successfully tested in laboratory animals for long periods of time (up to 776 days to date). The failure rate of ALCON PADs is 1 per 82 implant-months while in controls it is 1 per 7 implant-months. As a reference, the rate of exit site/tunnel infections for continuous ambulatory peritoneal dialysis (CAPD) patients reported by the NIH National CAPD registry[12] is 1 per 20 implant-months.

Once a long-term PAD is obtained, the potential medical uses are numerous[3]. Our laboratory developed and investigated the clinical application of a pneumatically powered partial mechanical heart, the dynamic aortic patch (DAP). This permanently implanted left ventricular assist device operates on the same principle as the intra-aortic balloon pump and has demonstrated its hemodynamic effectiveness over a 3 mo period in a patient in his own home setting[13-15]. The requirement for connection to an external pneumatic power source, however, makes an effective PAD necessary.

In order to confirm the ability of an ALCON PAD to maintain a tissue seal even when powering a functioning heart assist device (i.e. the DAP), a change in the experimental animal was desirable. The sheep was chosen. Initial histology is similar to that obtained from the swine. Our observation of PADs in the 2 sheep tethered to a drive unit (4 mos to date) is consistent with our expectations that once a seal between the PAD and the surrounding tissue is achieved, it will sustain the stress associated with energy transmission.

In addition, the feasibility of using the same culture technique for human fibroblasts taken from elderly donors (up to age 77) allows us to believe that the development of a PAD suitable for use in humans is practicable. Beyond its utility in conjunction with mechanical circulatory assistance systems, the potential clinical applications of a satisfactory long-term PAD extend to dialysis, skeletal attachment of prosthetic limbs, drug delivery, and other therapies.

CONCLUSION

A percutaneous access device, with a failure rate of 1 per 82 implant-months in swine shows promise as an effective means for transferring pneumatic power to an implanted heart assist system. The PAD is also potentially useful for continuous ambulatory peritoneal dialysis and other therapies.

REFERENCES

1. Miller J, Brooks CE. Problems related to the maintenance of chronic percutaneous electronic leads. J Biomed Mater Res Symposium (Part 1) 2:251, 1971.
2. Mooney V. Hartmann DB. Percutaneous passage. In: Miller HA, Harrison DC, eds. Biomedical Electrode Technology. New York: Academic Press, Inc., 1974, pp 329-339.
3. Von Recum A, Park JB. Permanent percutaneous devices. CRC Critical Reviews in Bioengineering 11:37, 1981.
4. Vaughan FL, Bernstein IS, Freed P, Kantrowitz A. The use of biological processes in the development of long-term percutaneous energy transmission system. In: Szycher M, ed. Biomedical Polymers, Metals, and Composites. Westport, CT: Technomic Publishing Co., Inc., 1983.
5. Hall CW, Ghidoni JJ. Indirect percutaneous cannula construction. J Surg Res 25:122, 1978.
6. Daly BDT, Dasse KA, Clay W, Poirier VL, Haudenschild CC, Fine RE, Robinson WJ, Ross JN, Szycher M, Worthington MB, Kayne HL, Lewis MB, Handrahan J. Development of percutaneous energy transmission systems. NHLBI Devices and Technology Branch Contractors Meeting. Dec 1984, 57.

7. Winter GD. Transcutaneous implants: Reactions of the skin-implant interface. J Biomed Mater Res Symposium 5:99, 1974.
8. Polanski J, Freed P, Wasfie T, Kantrowitz A, Vaughan F, Bernstam L, Gray R, Bernstein I. Inhibition of epithelial downgrowth on percutaneous access device in swine. Trans Am Soc Artif Intern Organs 29:569, 1983.
9. Wasfie T, Freed P, Hagiwara K, Vaughan F, Bernstam L, Gray R, Bernstein I, Kantrowitz A. Inhibition of epithelial downgrowth on percutaneous access devices in swine: II. Trans Am Soc Artif Intern Organs 30:556, 1984.
10. Vaughan FV, Freed PS, Yoshizu H, Hayashi I, Bernstam L, Gray RH, Brabec RK, Wasfie T, Polanski J, Bernstein IA, Kantrowitz A. Advances in percutaneous access device development. Trans Am Soc Artif Intern Organs 28:154, 1982.
11. Kantrowitz A, Freed PS, Ciarkowski AA, Hayashi I, Vaughan FL, VeShancey JI, Gray RH, Brabec RK, Bernstein IA. Development of a percutaneous access device. Trans Am Soc Artif Intern Organs 26:444, 1980.
12. Steinbert SM, Cutler SJ, Novak JW. Findings from NIH National CAPD Registry: January 1985. (Abstract) Am Soc Artif Intern Organs 14:41, 1985.
13. Kantrowitz A, Freed P, Wasfie T, Kozlowski J, Rubenfire M. Permanent cardiac assistance in chronic congestive failure by means of a mechanical auxiliary ventricle. Proc 5th Int Symp Hemoperfusion and Artif Organs. Tianjin, China, Nov 20-22, 1983 (in press).
14. Kantrowitz A, Krakauer JS, Zorzi G, Rubenfire M, Freed PS, Phillips S, Lipsius M, Titone C, Cascade P, Jaron D. Current status of the intraaortic balloon pump and initial clinical experience with an aortic patch mechanical auxiliary ventricle. Transplant Proc 3:1459, 1971.
15. Nelson R, Smith J, Drummond R, Pollard H, Billingsley J, Nikkila M. Care of a man with a partial artificial heart. Am J Nursing 73:1580, 1973.

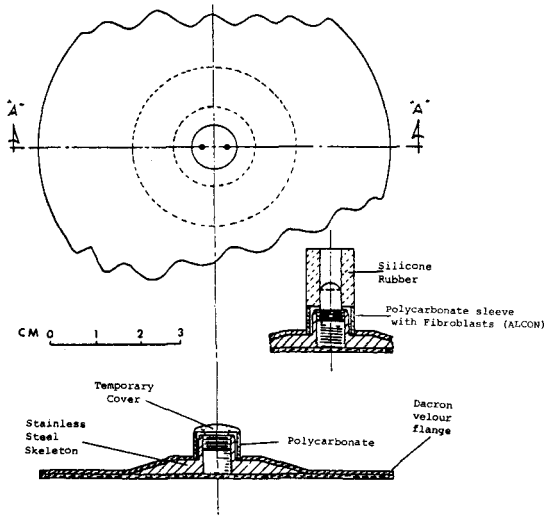

Figure 1. Simplified drawing of PAD showing internal construction.

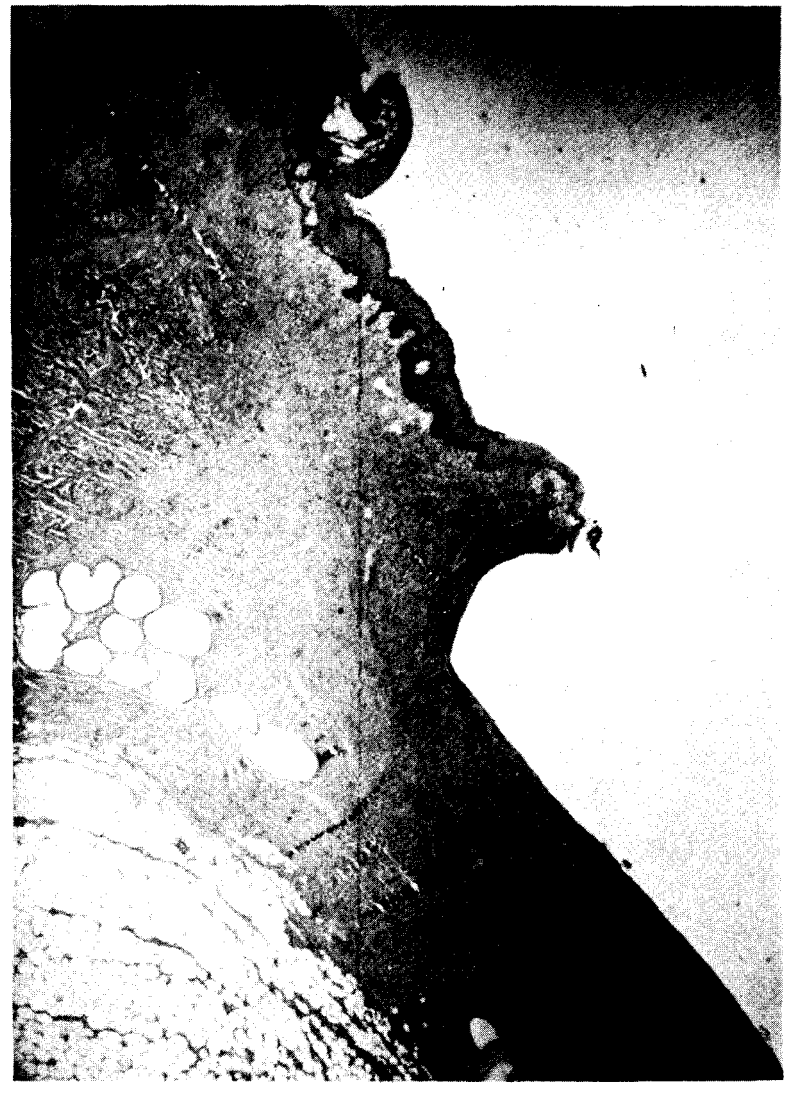

Figure 2. Histologic section of tissue-PAD interface removed from a swine, 140 days after implantation. It was explanted 2 days following trauma of unknown origin. The Lexan sleeve, which had been on the right, was dissolved to allow sectioning. Note the abrupt termination of the epidermis at the extension-sleeve junction.

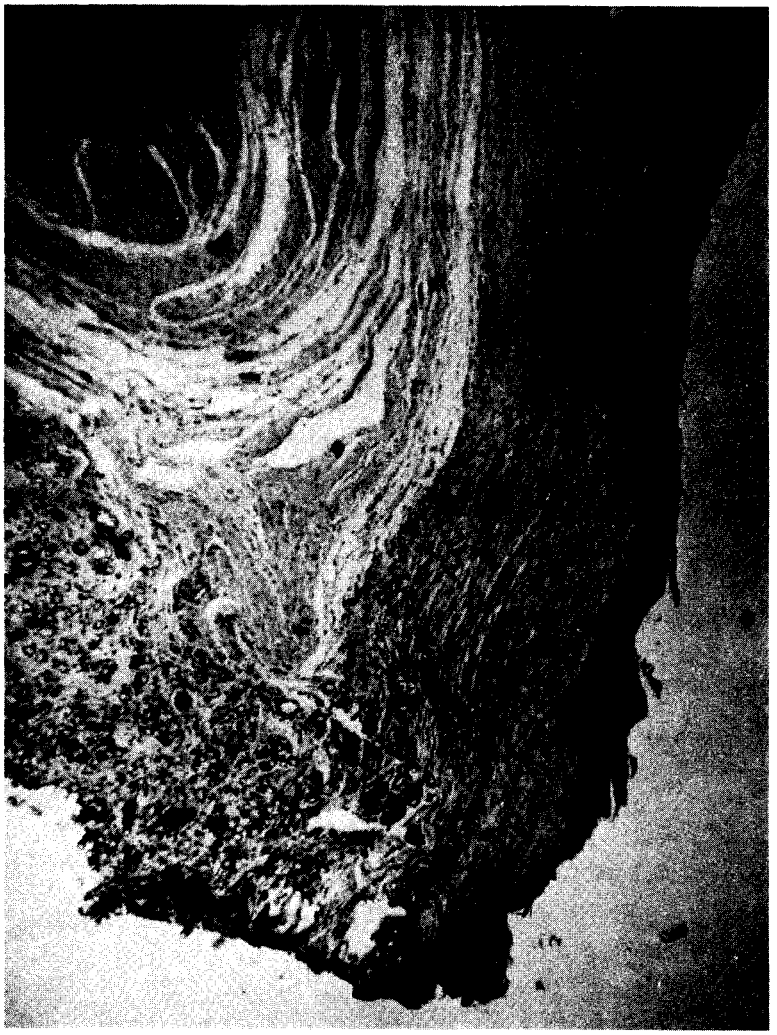

Figure 3. Histological section of skin in contact with a control PAD removed from left side of sheep #61, 5 wks after implantation, reveals a thin layer of epidermis growing to the level of the velour.

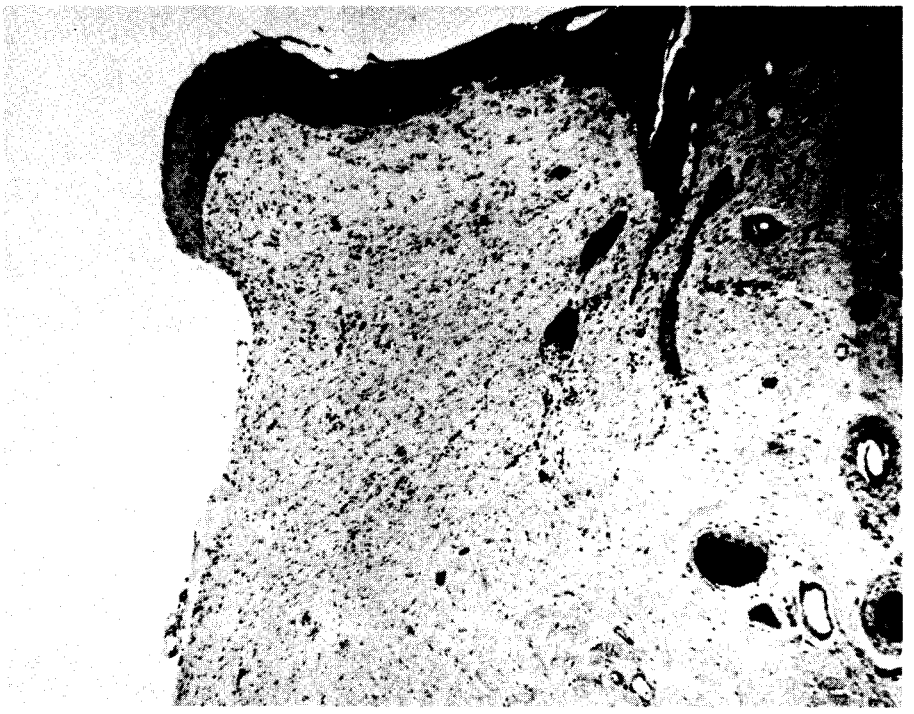

Figure 4. Histological section of skin in contact with ALCON PAD removed from the right side of sheep #61, 5 wks after implantation, showing abrupt termination of epidermis. The Lexan sleeve, which had been on the left of the picture, was dissolved to allow sectioning. Hematoxylin, Phloxine, and Saffron (reduced 20% from X175).